flask of suitable size to obtain a solution containing 0.3 milligram per milliliter of cefprozil (estimated) when diluted to volume with water. Filter through a 0.45 micron filter prior to injection into the chromatographic system.

(ii) *Calculations.* Calculate the cefprozil content as follows:

$$\text{Milligrams of cefprozil (Z) or cefprozil (E) per tablet} = \frac{A_u \times P_s \times d}{A_s \times 1{,}000 \times n}$$

$$\text{Milligrams of cefprozil per tablet} = \begin{matrix}\text{Milligrams of cefprozil (Z) per tablet} \\ + \\ \text{Milligrams of cefprozil (E) per tablet}\end{matrix}$$

where:

A_U=Area of the cefprozil (Z) or cefprozil (E) response in the chromatogram of the sample (at a retention time equal to that observed for the standard);

A_S=Area of the cefprozil (Z) or cefprozil (E) response in the chromatogram of the cefprozil (Z) or the cefprozil (E) working standard;

P_S=Cefprozil (Z) or cefprozil (E) activity in the cefprozil (Z) or the cefprozil (E) working standard solution in micrograms per milliliter;

d = Dilution factor of the sample; and

n = Number of tablets taken in the sample.

(2) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(3) *Dissolution test.* Proceed as directed in § 436.215 of this chapter. The quantity Q (the amount of cefprozil activity dissolved) is 75 percent at 45 minutes.

(4) *Identity*—(i) *High performance liquid chromatography.* Using the high performance liquid chromatographic procedure described in paragraph (b)(1) of this section, the retention times for the responses of the active ingredients must be within 2 percent of the retention times for the responses of the corresponding reference standards.

(ii) *Thin layer chromatography.* Proceed as directed in § 436.368 of this chapter.

[58 FR 26661, May 4, 1993]

§ 442.180b Cefprozil for oral suspension.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefprozil for oral suspension is cefprozil with one or more suitable and harmless preservatives, sweeteners, suspending agents, buffers, and flavorings. The cefprozil content of the oral suspension is satisfactory if it is not less than 90 percent nor more than 120 percent of the number of milligrams of anhydrous cefprozil that it is represented to contain. When constituted as directed in the labeling, each milliliter contains the equivalent of either 25 or 50 milligrams anhydrous cefprozil activity. Its moisture content is not more than 3 percent. When constituted as described in the labeling, the pH of the suspension is not less than 4.0 nor more than 6.0. It passes the identity tests. The cefprozil used conforms to the standards prescribed by § 442.80(a)(1) of this part.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(A) The cefprozil used in making the batch for potency, E-isomer ratio, moisture, pH, crystallinity, and identity.

(B) The batch for content, moisture, pH, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(A) The cefprozil used in making the batch: 10 packages, each containing approximately 500 milligrams.

(B) The batch: A minimum of 10 intermediate containers.

(b) *Tests and methods of assay*—(1) *Cefprozil content.* Proceed as directed in § 442.80(b)(1), preparing the sample solution and calculating the cefprozil content as follows:

(i) *Preparation of sample solution.* Constitute as directed in the labeling. Transfer a portion of the suspension containing 250 milligrams (estimated) of cefprozil into a 250-milliliter volumetric flask using a glass syringe and a 13-gauge needle. Dilute to volume with water, ultrasonicate briefly to dissolve and mix well. Transfer a 15-milliliter aliquot of this solution to a 50-milliliter volumetric flask and dilute to volume with water to obtain a solution containing 0.3 milligram per

milliliter of cefprozil (estimated). Filter through a 0.45 micron filter prior to injection into the chromatographic system.

(ii) *Calculations.* Calculate the cefprozil content as follows:

$$\text{Milligrams of cefprozil (Z) or cefprozil (E) per 5 milliliters of sample} = \frac{A_u \times P_s \times d \times 5}{A_s \times 1{,}000 \times V}$$

$$\text{Milligrams of cefprozil per 5 mL of sample} = \text{Milligrams of cefprozil (Z)/5 mL sample} + \text{Milligrams of cefprozil (E)/5 mL sample}$$

where:

A_U=Area of the cefprozil (Z) or cefprozil (E) response in the chromatogram of the sample (at a retention time equal to that observed for the standard);

A_S=Area of the cefprozil (Z) or cefprozil (E) response in the chromatogram of the cefprozil (Z) or the cefprozil (E) working standard;

P_S=Cefprozil (Z) or cefprozil (E) activity in the cefprozil (Z) or the cefprozil (E) working standard solution in micrograms per milliliter;

d = Dilution factor of the sample; and

V = Volume of sample taken in milliliters.

(2) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(3) *pH.* Proceed as directed in § 436.202 of this chapter, using the drug constituted as directed in the labeling.

(4) *Identity*—(i) *High Performance liquid chromatography.* Using the high-performance liquid chromatographic procedure described in paragraph (b)(1) of this section, the retention times for the responses of the active ingredients must be within 2 percent of the retention times for the responses of the corresponding reference standards.

(ii) *Thin layer chromatography.* Proceed as directed in § 436.368 of this chapter.

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Subpart C—Injectable Dosage Forms

§ 442.208 Cefamandole nafate for injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefamandole nafate for injection is a dry mixture of cefamandole nafate and one or more suitable and harmless buffering agents. The cefamandole nafate may be isolated in the manufacture of cefamandole nafate for injection. Its cefamandole content is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of cefamandole that it is represented to contain. It is sterile. It is nonpyrogenic. Its moisture content is not more than 3.0 percent. Its pH is not less than 6.0 and not more than 8.0. If isolated, the cefamandole nafate used conforms to the standards prescribed by § 442.8a(a)(1). If the cefamandole nafate is not isolated, the potency of the dry mixture is not less than 810 micrograms and not more than 1,000 micrograms of cefamandole per milligram on an anhydrous basis when corrected for sodium carbonate; and the dry mixture gives a positive identity test.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) If isolated, the cefamandole nafate used in making the batch for cefamandole content, moisture, pH, and identity.

(*b*) The batch for cefamandole content, sterility, pyrogens, moisture, and pH. In addition, if the cefamandole nafate is not isolated, results of tests and assays on the dry mixture for potency and identity.

(ii) Samples required:

(*a*) For all tests except sterility: A minimum of 10 immediate containers, unless the cefamandole nafate is not isolated, a minimum of 15 immediate containers.

(*b*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Cefamandole content.* Proceed as directed in § 436.324 of this chapter, preparing the sample solution and calculating the cefamandole content as follows:

(i) *Sample preparation.* Reconstitute the sample as directed in the labeling.